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EXAMINER	
SHAFER, SHULAMITH H	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,183	ULMANN ET AL.	
	Examiner	Art Unit	
	SHULAMITH H. SHAFER	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,11,14,24-28,34,40,46,49-51,53,57,59,62,64-67 and 74-80* is/are pending in the application.

4a) Of the above claim(s) *1-3,11,14,24-28,34,40,46,49,51,53,57-59 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50,64-67,74-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims:

Applicants' response of 12 April 2010 is acknowledged. Claims 50 and 78 have been amended and the amendment made of record. Claims 77-80 are newly presented and made of record.

Claims 1-3, 11, 14, 24-28, 34, 40, 46, 49-51, 53, 57, 59, 62, 64-67 and 74-80 are pending in the instant invention. Claims 1-3, 11, 14, 24-28, 34, 40, 46, 49, 51, 53, 57, 59, and 62 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 50, 64-67 and 74-80 are under consideration.

Withdrawn Objections

The objection to the title of the invention is withdrawn. Applicants have submitted a new title, thereby obviating the objection.

Applicants have amended the Specification at paragraphs [0006], [0012], [0017], and [0018] to add SEQ ID NOs: 36-106 to amino acid sequences that are listed in FIGS. 3, 9, 14, and 15 as originally filed. Applicants have also provided an amended "Sequence Listing" to reflect the addition of SEQ ID NOs: 36-106. Therefore, the objection to the specification as failing to comply with 37 C.F.R. § 1.821(d) is withdrawn.

Withdrawn Rejections

The rejection of Claims 50 and 64-67 under 35 U.S.C. 102(a) as being anticipated by Harborth et al. (2001. J. Cell Sci. 114:4557-4565) is withdrawn in light of Applicants' amendment to the claims. Claim 50, one of the independent claims of the instant invention, has been amended to recite "wherein the Nup153 inhibitor is a peptide". Harborth et al. teach using RNAi as an inhibitor of Nup 153 and thus does not anticipate the limitations of the pending claims.

Maintained/New Grounds of Objection/Rejection

Sequence Rules:

The specification is not in compliance with the requirements of 37 CFR 1.821 through 1.825 of the Sequence Rules and Regulations. Specifically the application fails to comply with CFR 1.821(e) and (f), which states:

(e) A copy of the "Sequence Listing" referred to in paragraph (c) of this section must also be submitted in computer readable form (CRF) in accordance with the requirements of § 1.824. The computer readable form must be a copy of the "Sequence Listing" and may not be retained as a part of the patent application file.
(f) In addition to the paper or compact disc copy required by paragraph (c) of this section and the computer readable form required by paragraph (e) of this section, a statement that the "Sequence Listing" content of the paper or compact disc copy and the computer readable copy are the same must be submitted with the computer readable form, e.g., a statement that "the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing."

Applicants have amended the specification to add SEQ ID NOs:36-106 and have also provided an amended "Sequence Listing" to reflect the addition of SEQ ID NOs:36-106. However, Applicants have not filed a computer readable form as required by section (e) and a statement that the "Sequence Listing" content of the paper or compact disc copy and the computer readable copy are the same must be submitted with the computer readable form, e.g., a statement that "the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing."

Applicant must submit a response to this Office Action and compliance with the sequence rules within the statutory period set for response to this Office Action

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

The rejection of Claims 50, 64-67 and 74-76 under 35 U.S.C. 112, first paragraph, is maintained and now applied to newly submitted claims 77-80 for reasons of record and for reasons set forth below. The specification, while being enabling for a method of inhibiting cell cycle of a cell *in vitro* comprising administering a Nup153 inhibitor to the cell, does not reasonably provide enablement for a method of inhibiting cell cycle of a cell *in vivo* comprising administering a Nup153 inhibitor to the cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to a method of inhibiting a cell cycle comprising administering a Nup153 inhibitor to a cell wherein the Nup153 inhibitor is a peptide. Given the broadest reasonable interpretation, the claims encompass administration of an inhibitor to an isolated cell, and to a subject comprising said cell (*in vivo* administration, as recited in claim 75). The claims are also broadly drawn to a method of treating cancer in a subject (as recited in claim 76).

The specification teaches a method of inhibiting a cell cycle of a cell comprising administering a Nup153 inhibitor to the cell in vitro [paragraph 0297 of PGPUB 20050226879, the PGPUB of the instant application]. The test system disclosed comprises cell free extracts derived from Xenopus eggs, which were used to form synthetic nuclei around sperm chromatin. When an inhibitor of Nup 153, a fragment encompassing the central zinc finger domain of Nup 153, was included in the cell free system, inhibition of nuclear envelope breakdown was apparent [paragraph 0038]. Antibodies that specifically recognize Nup153 were able to prevent the normal progression of events in nuclear envelope disassembly. The nuclear membrane stayed largely intact after administration of said antibodies to the cell free extracts [paragraph 0161]. The disclosure teaches that methods which inhibit nuclear envelope breakdown may inhibit cancer cell proliferation [paragraph 0026]. Methods of identifying compounds that inhibit nuclear envelope breakdown are taught [paragraphs 0267-0272]. The disclosure contemplates utilization of the identified compounds to treat a subject with cancer [paragraphs 0302-0304].

Working examples: Examples 1 and 2 teach incubation of Nup153 fragments (Example 1) or synthetic peptides (13-meres) (Example 2) with cell free extracts derived from *Xenopus* eggs; these extracts form synthetic nuclei around sperm chromatin. Administration of these inhibitors of Nup 153 inhibits the breakdown of the nuclear envelope. There are no teachings, working or prophetic, of administration of inhibitors of Nup153 to cancer cells *in vitro* or administration of Nup 153 *in vivo*.

In vivo administration of Nup153 inhibitors to inhibit a cell cycle of a cell or to inhibit a cell cycle of a cancer cell is not enabled for the following reasons:

The teachings in the specification provide insufficient guidance and objective evidence to predictably enable the use of the claimed methods *in vivo*. *In vitro* assays, as detailed in the disclosure of the instant application are useful in determining basic physiological phenomena and in screening the effects of potential therapeutic compounds. However, clinical correlations are generally lacking. The greatly increased complexity of the *in vivo* environment as compared to the controlled conditions of an *in vitro* assay does not permit a single extrapolation of in vitro assays to human treatment

efficacy with any reasonable degree of predictability. It is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicated the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interactions. "There have been major advances in the use of cell culture and recombinant human cells, and *in silico* approaches are also providing valuable alternatives to animal experiments by simulating drug interaction and response data. But, these studies still cannot predict the integrated response of a potential drug as accurately as living systems, in which a combination of genetic, biochemical, physiological, pathological and environmental influences work in concert" (Frantz. Nature Rev. Drug Dis. 2003. 2:501, 1st column, 3rd paragraph). Additionally, the nature of the invention is complex, involving the effects of proteins on biological systems. It is noted that the courts have long settled that such is considered complex. See Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), wherein it was determined that a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amqen Inc. v. Chuqai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991).

Due to the large quantity of experimentation necessary to determine if administration of Nup153 inhibitors, wherein said inhibitors are peptides, *in vivo* would be effective in inhibiting cell cycle progression, and thus be effective in treating cancer in a subject, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of treatment of cancer in a subject and the breadth of the claims which fail to recite any limitations as to *in vitro*, undue experimentation would be required of the skilled artisan to practice the claimed invention in its full scope.

Applicants traverse the rejection (Response of 12 April 2010, page 10, 2nd and 3rd paragraphs). The reasons for the traversal are:

Applicants have amended Claim 50 to recite a method of inhibiting a cell cycle of a cell comprising administering a Nup153 inhibitor to the cell, wherein the Nup153 inhibitor inhibits the cell cycle of the cell, wherein the Nup153 inhibitor is a peptide. Applicants submit that even if experimentation might be required to perform the claimed method, then such experimentation would not be undue. Applicants submit that, at the time of the filing, the art was familiar with making therapeutic peptides, testing therapeutic peptides, administering a therapeutic peptide to a subject to achieve a desired result, and adjusting the administration of a therapeutic peptide to a subject to achieve maximum efficacy. Thus, Applicants' Specification bears more than a "reasonable correlation" to the scope of the currently pending claims.

Applicant's arguments have been fully considered but have not been found to be persuasive.

Applicants claims are directed to a novel target for inhibition of cell cycle progression, and cell proliferation and thus a novel therapeutic target for treatment of cancer. However, the specification has presented insufficient direction which would allow one of ordinary skill to predict that administration of peptide inhibitors of Nup153 would be effective to inhibit cell cycle. The question is not how to make and administer therapeutic peptides, but whether the administration of peptides which inhibit Nup153 in vivo would be effective in inhibition of cell cycle progression, cell proliferation and therefore would be effective in treatment of cancer.

As discussed above, Applicants have only taught methods of inhibiting a cell cycle in a cell by administering a Nup 153 inhibitor to a cell extract and to cell culture systems, that is, *in vitro*. However, the narrowly defined and controlled conditions of an in vitro assay system does not permit a single extrapolation of in vitro assays to human therapeutic efficacy with any reasonable degree of predictability. No model that can reasonably be correlated to the breadth of the claimed method has been presented. Preclinical cancer models, principally *in vitro* cell studies, have long been understood to have a particularly poor track record and, specifically, do not correlate with actual success in the treatment of cancer. The standard models for testing cancer drugs include cultured human tumor cell lines. One problem with these models is the artificial

nature of tumor cell lines that are typically passaged for many generations in culture and which may not be representative of the tumor in its native state. Cells in culture lack the architectural and cellular complexity of real tumors, which incorporate inflammatory cells, vasculature and other stromal components (Kamb. Nature Rev. Drug Discovery. 2005:4:161-165, page 162, 2nd column, last paragraph). A direct measure of the low predictive value of preclinical screening for anti-cancer drugs is the low rate of response for Phase 1 clinical trials. Roberts, Jr et al., *JAMA* 292(17): 2130-2140 (2004), Table 4, shows response rates for the 1999-2002 period ranging from 0.4% to 5.3%; the overall response rate was 3.8%. Percentages this low clearly indicate that the pre-clinical screening as a whole is absolutely not predictive --- even a rate 10 times that high would indicate that the preclinical tests are not reliably predictive.

In view of the discussion above, undue experimentation would be required of the skilled artisan to practice the claimed invention in its full scope; the rejection is therefore maintained.

Written Description

Claims 50, 64-67, and 75-80 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim (s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Written Description Training Materials, Revision 1, March 25, 2008.

Claims 50, 64-67, 75, and 76 are directed to a method comprising administration a Nup153 inhibitor, wherein the Nup153 inhibitor is a peptide; newly submitted claims 77-80 recite a method of inhibiting a cell cycle of a cell comprising administration of a Nup153 inhibitor.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or

she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117).

With respect to claims 50, 64-67, 75, 76 and 80:

A review of the language of the claim indicates that these claims are drawn to a method comprising administration of a genus, i.e., peptides which inhibit Nup153

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states, "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

The specification discloses the following information about a Nup153 inhibitor, wherein the inhibitor is a peptide:

A fragment encompassing the central zinc finger domain of Nup153 inhibits the breakdown of nuclear envelope when included in cell-free extracts derived from Xenopus eggs, which were used to form synthetic nuclei around sperm chromatin [paragraph 0038].

The inhibitory composition can bind a peptide, wherein the peptide comprises a sequence having at least 30%, 40%, 45%, 46%, 47%, 48%, 49%, 50%, 60%, 70%, 80%, 90%, or 100% identity to amino acids 658 to 891 of SEQ ID NO: 2 (the zinc finger domain of Nup153) [paragraph 0041]; however the structure of the binding peptide is not further disclosed nor is any relationship between the structure of the peptide and the ability to bind SEQ ID NO:2 described.

The inhibitors of nuclear envelope breakdown, such as inhibitors of Nup153-COPI interaction may have a relationship to the zinc finger region of Nup153. This region contains 5 zinc fingers connected by a variety of different linking regions. Thus, in certain embodiments two or more zinc fingers can be linked together to form an inhibitor. Molecules have this type can be represented by the formula I

$$-((Z_{.a}\text{-}L_{.a}\text{-}Z_{.b})\text{-}L_{.b})_n$$

Wherein - $Z_{.a}$ and $Z_{.b}$ represents a zinc finger

Wherein -$L_{.a}$ and $L_{.b}$ represents a linker which can be anything [paragraphs 0044-0050]

Inhibitory compositions that interact with the zinc finger region of Nup153, may be identified using any selection mechanism, such as phage display or a two-hybrid system. For example, CTTHPFTHECGGGS (SEQ ID NO: 30) was identified in a phage display experiment to a Nup153 zinc finger. This peptide in synthetic form as well as displayed form was capable of inhibiting nuclear envelope breakdown [paragraph 0053].

Antibodies that specifically recognize Nup153 were used in a nuclear disassembly assay. One antibody recognized the zinc finger region, and the other N-terminal region. Both antibodies were able to prevent the normal progression of events in disassembly [paragraph 0161 and Example 1].

Thus, the following species are within the scope of the claimed genus: fragments encompassing the central zinc finger domain of Nup153, the synthetic peptide of SEQ ID NO:30 and antibodies that specifically recognize Nup153. The disclosure of a few species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claims encompass numerous species (unspecified peptides) that are not further described.

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is peptides which inhibit Nup153. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

With respect to claims 77-79:

The claims recite administration of a Nup153 inhibitor, wherein the Nup153 inhibitor interferes with a Nup153-COPI interaction.

A review of the language of the claim indicates that these claims are drawn to a method comprising administration of a number of genera: compounds which interfere with Nup153-COPI interaction.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117).

To provide adequate written description and evidence of possession of a claimed genus or claimed genera, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicant has identified the composition to be administered only by description of a function, the ability to interfere with Nup153-COPI interaction. However, the inhibitor

is not further described by any common structural characteristics or structural/functional relationships.

In the instant application, the specification discloses a wide variety of compounds of different structural and functional characteristics which may exhibit the required functionality: inhibition of Nup153-COPI interaction. These compounds include, but are not limited to, a fragment encompassing the central zinc finger domain of Nup153 [paragraph 0038], variants of the Nup153 protein and derivatives of these proteins [paragraph 0140], chimeric proteins [paragraph 0191], antibodies to Nup153 [paragraph 0051, 0160], functional nucleic acids including antisense molecules, aptamers, ribozymes, triplex forming molecules, external guide sequences [paragraph 0087], RNA interference molecules (RNAi) or small interfering RNA (SiRNA) [paragraph 0092], small molecules [paragraph 0192], flavenoids [paragraph 0194] and synthetic peptides [paragraph 0359]. The specification teaches a single species of each of the following genera: variants of Nup153 (species: a fragment encompassing the central zinc finger domain of Nup153), antibodies (species: antibodies specific to Nup153), and synthetic peptides (species: CTHPFTHECGGGS, SEQ ID NO: 30) as meeting the functional limitation stated in the claim.

Applicant has failed to provide any written description of most of the genera encompassed by the claim (variants of the Nup153 protein and derivatives of these proteins, chimeric proteins, and functional nucleic acids including antisense molecules, aptamers, ribozymes, triplex forming molecules, external guide sequences, RNA interference molecules (RNAi) or small interfering RNA (SiRNA), small molecules) and has only provided adequate description of a single species within each of three broad genera, as discussed above.

Claim 77 is thus a single means claim wherein the claim covers every conceivable structure (means) for achieving the stated purpose (inhibiting a cell cycle) but the specification at most discloses only three compositions.

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genera, which are inhibitors of inhibition of Nup153-COPI interactions. One of skill in the art would not

recognize from the disclosure that the applicant was in possession of the genera. Therefore, only the following compounds: a fragment encompassing the central zinc finger domain of Nup153, antibodies specific to Nup153, and the synthetic peptide of SEQ ID NO:30 but not the full breadth of the claim meets the written description provision of 35 U.S.C. 112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Conclusion:

No claims are allowed

In light of new grounds of rejection, this Action is non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D. can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shulamith H. Shafer/

Examiner, Art Unit 1647